which is the same as the attached paper copy. Submission of the Sequence Listing does not add new matter as the sequence information contained therein was presented in the application as originally filed.

New claims 16-19 have been added and claims 11 and 13-15 have been revised to depend from claim 16. Support for the new claims can be found, for example, at pages 30 and 31 of the application.

The Abstract has been revised so as to correspond to the claimed invention.

Claims 1-8, 9, 11 and 13-15 stand rejected under 35 USC 112, first paragraph (it is believed claims 8, 9, 11 and 13-15 were intended). Withdrawal of the rejection is submitted to be in order for the reasons that follow.

The Examiner indicates that Applicants have not disclosed how to use CD44-specific antibodies therapeutically in mammals. The Examiner then goes on to comment on an alleged lack of correlation between *in vitro* and *in vivo* operability of the claimed therapeutic strategy. The Examiner further states that, in the area to which the invention relates, *in vitro* and animal studies have not correlated well with clinical trial results in humans.

The Examiner's comments would appear to relate more properly to a rejection under 35 USC 101 than 35 USC 112. Such a

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rejection was previously made in this case, but was subsequently withdrawn. Accordingly, the record indicates that the question of utility has been adequately addressed and comments relating, for example, to correlations between models and humans and the "asserted operability" of the claimed invention are no longer appropriate.

The subject specification teaches how to make and how to use the invention in that it fully discloses how to make the anti-CD44 antibodies and how to use those antibodies to inhibit infection of cellular targets (eg mononuclear phagocytes - see particularly claims 13 and 14 and new claims 16-19) both *in vivo* and *ex vivo* .

One skilled in the art would appreciate that for *in vivo* treatment, intravenous administration is appropriate. For *ex vivo* use (see page 30 of application, last paragraph), the agent can be mixed with a potentially infected product (eg blood, blood plasma, or purified blood factor) before administration to the patient. *Ex vivo* mixing would prevent infection of host cells by the administered product. For topical treatment, the agent can be administered in a solution (eg liquid or gel or foam form) within a condom or to a mucosal surface (see page 30 of application, lines 20-22). So administered, HIV infection of the mononuclear phagocytes (eg on mucosal surfaces) can be inhibited.

Optimum formulations and dosing regimens to be used can be readily established by one skilled in the art - no undue experimentation would be required. Indeed, the Examiner has not indicated why such would not be the case. The Examiner is requested to point out what further teachings relating to "how to make" and/or "how to use" the invention are necessary, or withdraw the rejection.

The Examiner is particularly requested to note that claim 13 relates to inhibition of HIV infection of mononuclear phagocytes and claim 14 recites human monocytes (see also the new claims). The manuscript of Rivadenevia relates specifically to the inhibition of HIV infection of mononuclear phagocytes and indeed the Examiner acknowledges the positive results presented therein. The Examiner appears to fault the document for not showing 100% effectiveness using the CD44-specific antibodies. The Examiner is reminded that such levels are not required to satisfy the requirements of 35 USC 112 and that, indeed, many commercially important drugs are not 100% effective.

Summarizing, the subject specification adequately teaches how to make and how to use the invention. Further, the operability of the claimed method would be believable on its face to one skilled in the art. The Examiner has acknowledged this to be the case by withdrawing the rejection under 35 USC 101.

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The Examiner also contends that the subject specification does not provide a method of obtaining A3D8 and A1G3 antibodies. These antibodies have been widely distributed and have been the subject of a variety of publications, their preparation having been described initially by Haynes et al, J. Immunol. 131:1195-1200 (1983) and Telen et al, J. Clin. Invest. 71:1878-1886 (1983) (copies to follow). They have been commercially available prior to April 1991, for example, from Sigma Chemical Co. Given the ready availability of the antibodies and their distribution to date, no deposit for patent purposes should be necessary.

In view of the above, reconsideration is requested.

Claim 11 stands rejected under 35 USC 112, second paragraph, as allegedly being indefinite. Withdrawal of the rejection is in order for the reasons that follow.

The designations to which the Examiner refers are in no way indefinite. On page 13 of the application, lines 17-20, the relevant publications (mentioned above) are cited. Accordingly, the identity of the antibodies would be absolutely clear.

Reconsideration is requested.

Claims 1-8, 9, 11 and 13-15 stand rejected under 35 USC 103 as allegedly being obvious over Willerford et al or Landay et el in view of Nicholson et al and Matsushita et al (it is believed that claims 8, 9, 11 and 13-15 were intended). Withdrawal of the rejection is submitted to be in order in view of the above-noted

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claim amendments and for the reasons that follow. Attention is particularly directed to the fact that new claim 16 has been added and that claims 11 and 13-15 now depend therefrom. The rejection is not believed to applicable to claim 16 or claims depending therefrom.

At the outset, it is noted that the combination upon which the Examiner relies in rejecting the claims could only have been constructed having in mind the present invention. That type of retrospective reasoning is, of course, improper.

The present invention relates to a method of inhibiting HIV infection. The invention results from Applicants' observation that CD44 facilitates HIV infection in human cells. When the molecule is "blocked", for example, by binding of an anti-CD44 antibody, HIV infection is inhibited. Claim 16 makes it clear that the antibody of the claim exerts its inhibitory effect by "blocking" the the CD44 molecule.

In rejecting the claims as obvious, the Examiner appears to be suggesting that the claims encompass methods of inhibiting HIV infection by killing surrounding HIV infected cells. It is respectively submitted that such an interpretation can only result from a very strained reading of the claims. It is further submitted that claim 16 as now presented precludes such an interpretation.

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The following comments are offered for purposes of clarifying the distinction between the cited art and the claimed invention.

The primary references upon which the Examiner relies teach CD44 cells as reservoirs of HIV infection. The references are in fact irrelevant to the claimed invention as they do not relate to inhibition of infection or prevention of spread of infection in an infected individual with any agent much less anti-CD44 antibodies.

Nicholson et al, like the primary references, fails to suggest the use of anti-CD44 antibodies as an agent for inhibiting HIV infection.

Matsushita et al relates to the use of immunotoxins to kill HIV infected cells. These teachings are completely unrelated to the present invention which, as should be clear from claim 16, relates to a method of inhibiting CD44-facilitated HIV infection of cells by "blocking" with an anti-CD44 antibody. Prevention of infection of CD44 cells is clearly preferred over killing since, if one were to follow what the Examiner views as the suggestion of the references, one would cause all CD44 cells to be killed which would result in a profound immunodeficiency. Clearly, such an approach is impractical.

In view of the above, it should be clear that the Examiner has relied on a strained reading of the claims to concoct a hindsight-based rejection. The Examiner is urged to reconsider

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his position and would believe that, having done do so, he will find withdrawal of the rejection to be in order.

This application is submitted to be in condition for allowance and a Notice to that effect is respectfully requested.

Respectfully submitted,

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